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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/621,268	07/21/2000	STEPHEN D. GILLES	LEX-007	3473

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EXAMINER	
PRASAD, SARADA C	
ART UNIT	**PAPER NUMBER**
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/621,268	Applicant(s) Gilles et al.	
	Examiner Sarada C Prasad	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26,44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

1. Receipt of Applicants' arguments and amendments filed in Paper No. 6 (10/11/01) is acknowledged. Claims 1-26 and 44-45 are under consideration.

2. The following previous rejections and objections are withdrawn in light of Applicants' amendments filed in Paper No. 6 (10/11/01).

(i) the rejection of claims 1-26, 44 and 45 under 35 U.S.C. 112-first paragraph;

(iii) the rejection of claims 1-26, 44-45 under 35 U.S.C. 103(a) as being unpatentable over Harvill et al. in view of U.S. Patent No. 5,349,053.

3. The issues remaining and new issues, are stated below.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112-second para

5. Claims 44-45 are rejceted under 35 U.S.C. 112, second paragraph, as being vague and indefinite based on recitation of 'fusion proteins comprising localizing protein..'.

This rejection of record is being maintained for reasons of record described in an earlier office action Paper No. 4 (4/10/10).

5a. Claims 44 and 45 reciting 'localizing protein' are vague and indefinite because it is not clear as to what characteristics that define a localizing protein, and localizing to what.

5b. Claims 1, 15, 44, 45 are vague and indefinite in reciting 'preselected antigen'. It is unclear as to what characteristics exactly define and control selection of the preselected antigen in the instant invention.

Claim Rejections - 35 USC § 103

6. Claims 1-26, and 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,349,053 (9/20/94), in view of Harvill et al. (1996).

U.S. Patent No.5,349,053 (Landolfi) teaches chimeric ligand/immunoglobulin molecules and their uses (title). In particular, the disclosure of Landolfi shows chimeric molecules having a ligand component linked to an immunoglobulin constant region component that can exhibit a high degree of specificity associated with the ligand, yet retain various effector functions characteristic of immunoglobulin heavy chains (abstract, lines 4-7, and column 2, summary, 1st para, lines 1-3). Teachings of Landolfi also include the constant region component is derived more preferably from a human IgG1 heavy chain, such as CH1 domain, hinge region, a CH2 region and/or a CH3 domain (lines 6-end of para). Their teachings also include that the ligand component of the immunoligand can be derived from any ligand molecule, such as interleukin-2, or portion thereof, with the ligand component is typically linked to the constant region component by a peptide bond (2nd para of summary, column 2, lines 4-end). Landolfi also discloses that the fusion protein also retains the properties of the ligand as well as the immunoglobulin region fused to it. These teachings meet the limitations of instant claims in preparing fusion proteins of preselected antigens using constant regions of immunoglobulins.

However, Landolofi did not teach use of these fusion proteins for immunization to elicit a stronger immune response. Harvill et al. demonstrated construction of an IgG3-IL-2 fusion protein that combines the antigenic moiety, effector functions of IgG3 with the immune stimulatory activities of IL-2 (page 3166, column 2, lines 1-3). Harvill et al. also pointed out that the large increase in Ab production in mice immunized with anti-DNS-IgG3-IL-2 bound Ag

suggests that this approach to vaccination may be successful with a wide variety of antigens (4th para, page 3169, lines 1-4). Disclosure of Harvill et al. also pointed out that the IgG3 fusion protein was also found to be unique among all the IgGs in having an extended hinge region of 62 amino acids that serves as a spacer separating the Fab from the Fc to which IL-2 is attached. Harvill et al. also expressly point out the role of the locator molecule in the fusion protein that would assist in colocalizing the antigen fusion protein and the adjuvant fusion protein to same or similar antigen presenting cells. However, neither Landolfi nor Harvill et al. taught to envision that adjuvanting cytokines as fusion proteins distinct from that of the antigen fusion protein and they be administered simultaneously or one after the other.

At the time the invention was made, with the knowledge that cytokines, such as IL-2, can fit the role of ligands as well as adjuvants, it would have been obvious to one of skill in the art to test cytokines other than IL-2 as adjuvants in combination with several preselected antigens for potential enhancement in antibody titre. Therefore, it would have been prima facie obvious to one of skill in the art, to combine the teachings of U.S. Patent No.5,349,053 and Harvill et al. to achieve the combined benefit of preparing antigen fusion proteins with enhanced stability and solubility in the form of Fc-antigens, while retaining the adjuvant choices in the form of distinct F-adjuvant proteins with their localizing function intact, and at the same time, achieving enhanced immunogenecity of pre-selected antigens, thus rendering obvious the methods recited in claims 1, 2, 4-26, 44 and 45.

The motivation for using prostate specific antigen, or cytokine or viral protein, and a tumor specific protein is provided by the need to obtain antibodies for use in therapy of cancer of these various types thereby making claims 10 and 22 obvious. Preparation of distinct fusion

proteins with various pre-selected antigens and various cytokine-adjuvant proteins would be advantageous to try various combinations of the different fusion proteins for quantitating the effective enhancement of immunogenicity. Therefore it would have been obvious to prepare different fusion proteins for the antigen and the adjuvant protein rather than a single fusion protein for antigen-adjuvant-Ig constant region, thereby making claims 1, 2, 15, 44 and 45 obvious.

The pharmaceutical composition of claims of 15, 44 and 45 are obvious over claim 12 of U.S. Patent No. 5,349,053 because the patented claim teaches compositions of immunoligands made up of fusion proteins with a suitable carrier. It would be obvious to include two fusion proteins in one composition instead of one fusion protein in one composition because such a composition would include the benefits of both having the antigen and the adjuvant as separate components for testing the mix and match combinations.

Conclusion

7. No claims are allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday – Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceedings should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.
Examiner Art Unit 1646
December 21st, 2001

YVONNE EYLER, PH.D
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